



## XPA gene

XPA, DNA damage recognition and repair factor

### Normal Function

The *XPA* gene provides instructions for making a protein that is involved in repairing damaged DNA. DNA can be damaged by ultraviolet (UV) rays from the sun and by toxic chemicals, radiation, and unstable molecules called free radicals.

DNA damage occurs frequently, but normal cells are usually able to fix it before it can cause problems. One of the major mechanisms that cells use to fix DNA is known as nucleotide excision repair (NER). As part of this repair mechanism, the XPA protein helps verify DNA damage and stabilize the DNA as it is repaired. The XPA protein attaches (binds) to areas of damaged DNA, where it interacts with many other proteins as part of a large complex. Proteins in this complex unwind the section of DNA where the damage has occurred, snip out (excise) the abnormal section, and replace the damaged area with the correct DNA.

### Health Conditions Related to Genetic Changes

#### xeroderma pigmentosum

At least 25 mutations in the *XPA* gene have been found to cause xeroderma pigmentosum. Mutations in this gene are responsible for a very severe form of the disorder that is more common in the Japanese population than in other populations. Most Japanese people with xeroderma pigmentosum have the same *XPA* gene mutation, which is written as IVS3AS, G>C. This mutation prevents cells from producing any functional XPA protein. Other *XPA* gene mutations, which have been reported in Japan and elsewhere, result in the production of a defective version of the XPA protein or greatly reduce the amount of this protein that is made in cells.

A partial or total loss of the XPA protein prevents cells from repairing DNA damage normally. As a result, abnormalities accumulate in DNA, causing cells to malfunction and eventually to become cancerous or die. These problems with DNA repair cause people with xeroderma pigmentosum to be extremely sensitive to UV rays from sunlight. When UV rays damage genes that control cell growth and division, cells can grow too fast and in an uncontrolled way. As a result, people with xeroderma pigmentosum have a greatly increased risk of developing cancer. These cancers occur most frequently in areas of the body that are exposed to the sun, such as the skin and eyes.

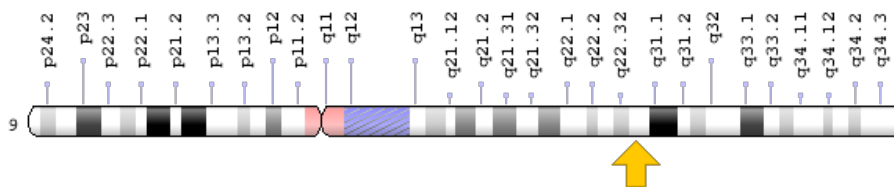
When xeroderma pigmentosum is caused by *XPA* gene mutations, it is often associated with progressive neurological abnormalities. These nervous system

problems include hearing loss, poor coordination, difficulty walking, movement problems, loss of intellectual function, difficulty swallowing and talking, and seizures. The neurological abnormalities are thought to result from a buildup of DNA damage, although the brain is not exposed to UV rays. Researchers suspect that other factors damage DNA in nerve cells. It is unclear why some people with xeroderma pigmentosum develop neurological abnormalities and others do not.

## Chromosomal Location

Cytogenetic Location: 9q22.33, which is the long (q) arm of chromosome 9 at position 22.33

Molecular Location: base pairs 97,654,398 to 97,697,409 on chromosome 9 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

## Other Names for This Gene

- xeroderma pigmentosum, complementation group A
- XP1
- XPA\_HUMAN
- XPAC

## Additional Information & Resources

### Educational Resources

- Cancer Medicine (sixth edition, 2003): Steps in Nucleotide Excision Repair (image) <https://www.ncbi.nlm.nih.gov/books/NBK13017/?rendertype=figure&id=A5537>
- Molecular Biology of the Cell (fourth edition, 2002): DNA Repair <https://www.ncbi.nlm.nih.gov/books/NBK26879/>
- Xeroderma Pigmentosum Society, Inc.: DNA Repair Explained in Simple Terms <https://www.xps.org/single-post/2015/04/08/DNA-Repair-Explained-in-Simple-Terms>

### GeneReviews

- Xeroderma Pigmentosum  
<https://www.ncbi.nlm.nih.gov/books/NBK1397>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28XPA%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

### OMIM

- XPA GENE  
<http://omim.org/entry/611153>

### Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
<http://atlasgeneticsoncology.org/Genes/XPAID104.html>
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=XPA%5Bgene%5D>
- HGNC Gene Family: Xeroderma pigmentosum complementation groups  
<http://www.genenames.org/cgi-bin/genefamilies/set/1125>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=12814](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=12814)
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/7507>
- UniProt  
<http://www.uniprot.org/uniprot/P23025>

### **Sources for This Summary**

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